Factors influencing diagnostic yield by directed endoscopic biopsy and cytology were studied in 50 patients with advanced gastric cancer using a forward-viewing panendoscope. The diagnostic yield was higher for exophytic lesions than for infiltrative tumor, and directed brush cytology alone was more productive than directed biopsy alone. The lesions that provided non-diagnostic tissue were mostly recurrent or infiltrative cancers, and were most often in the cardia, antrum, or were of the linitis plastica type. The combination of infiltrative character and location in antrum or cardia, especially if recurrent, often resulted in non-diagnostic biopsy and cytology specimens.

Although the incidence of gastric cancer is decreasing in this country, it, nevertheless, still accounts for more than 14,000 deaths per year. This annual mortality is comparable to that for cancer of the uterus, ovary, prostate, urinary tract, central nervous system, the malignant lymphomas, and leukemia. Unfortunately, in this country approximately 82% of gastric cancers are detected in a non-localized stage with lymph node metastases. It has been our clinical impression that within this group of advanced gastric cancers there are some that are hard to diagnose histologically. In the present study we have evaluated factors that appear to have a major bearing on our endoscopic diagnostic yield.

Methods and Patients

From among 356 consecutive upper gastrointestinal endoscopies performed by the Gastroenterology Service at Memorial Sloan-Kettering Cancer Center, those with proven gastric cancer were included. Endoscopies and directed biopsy and cytology procedures were generally performed by gastroenterology trainees under the supervision of experienced attending gastroenterologists. End-viewing fiberoptic panendoscopes (ACMI FO 7089P) were used in all cases. Directed biopsy and brush cytology specimens were obtained in all patients, except when contraindicated by coagulation defects. Four biopsy specimens were obtained per patient. A
standard cytology brush within a sheath was used to the point of slight bleeding. Slides were prepared from brushings in the endoscopy suite and immediately placed in 95% alcohol without prior air-drying. Biopsies were mounted on Gelfoam and placed in 10% buffered formalin. Tumors were classified according to their endoscopic appearance into two types of local growth patterns: exophytic, and infiltrative, if only thickened folds with an abnormal mucosal surface were present or lesions were flat. There were too few cases that involved the differential diagnosis of benign gastric ulcer to be included. When ulceration was present, it was never predominant. There were no patients with early gastric cancer in this series. All patients had invasion of cancer through serosa.

Results

Out of 356 patients who had endoscopies, there were a total of 85 patients with malignant tumors, including 63 patients with gastric adenocarcinoma. A correct visual diagnosis of cancer was made in 57 of 63 patients (90%). Of these 63 patients, 50 had both biopsy and cytology studies done and were selected for comparison.

There were 26 exophytic and 24 infiltrative cancers; 39 were primary and 11 were recurrent. Their anatomical locations in the stomach were: cardia, 15; body, 22 (including the 11 recurrent cancers); antrum, 7; and diffuse linitis, 6 (table 1). Cytological and/or histological confirmation of carcinoma was obtained in 92% of the exophytic tumors but in only 50% of those that were infiltrative, for an overall yield of 72% (table 2). Comparison of directed biopsy and brush cytology specimens showed a positive yield of 85% for brush cytology alone compared to 65% for biopsy alone in exophytic lesions, and 50% for brush cytology alone compared to 33% for biopsy alone in infiltrative lesions. The overall yield for brush cytology alone was 68% compared to 50% for biopsy alone (table 3).

Analysis of cases that failed to be diagnosed by both cytology and biopsy specimens revealed: 3 of 22 located in the body, all 3 being in patients with recurrent cancer; 3 of 7 located in the antrum; 4 of 6 with linitis plastica; and 4 of 15 located at the cardia (table 1). There were two exophytic lesions, one at the cardia and one that was recurrent. Twelve tumors were infiltrative, 2 were recurrent, 4 were linitis plastica, 3 were in the antrum, and 3 were at the cardia (table 1).

Discussion

The diagnosis of gastric cancer has been considerably improved by the application of directed endoscopic biopsy and brush cytology. Combined use of these procedures has been reported to result in histological confirmation of cancer in over 90% of reported cases. However, much of the literature is based on early gastric cancer. It has been appreciated that advanced gastric cancer often provides a lower diagnostic yield. In the present study, certain factors appeared to correlate with the diagnostic yield. One such factor was the gross

<table>
<thead>
<tr>
<th>Cardia</th>
<th>Primary</th>
<th>Recurrent</th>
<th>Body</th>
<th>Primary</th>
<th>Recurrent</th>
<th>Antrum</th>
<th>Linitis plastica</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>11</td>
<td>1</td>
<td>22</td>
<td>19</td>
<td>1</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Positive biopsy and/or cytology</td>
<td>1</td>
<td>3</td>
<td>11</td>
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<td>0</td>
<td>0</td>
<td>2</td>
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</table>

<table>
<thead>
<tr>
<th>Exophytic cancers</th>
<th>Infiltrative cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>50</td>
</tr>
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</table>
tumor growth pattern. Whereas exophytic mass tumors provided a correct diagnosis in 92% of the patients, infiltrative tumors provided a correct diagnosis in only 50%.

The influence of tumor growth pattern on diagnosis was also observed by Yamakawa and co-workers who reported that elevated lesions of early gastric cancer resulted in a higher biopsy yield than did depressed lesions.

Anatomical distribution of the tumor also correlated with the diagnostic yield. The combination of an infiltrative tumor and a location at the cardia or in the antrum behind the incisura resulted in a greater possibility of non-diagnostic biopsy and cytology specimens. These areas have been known in the past to present diagnostic difficulties. Most endoscopists appreciate the technical difficulties of obtaining multiple samples precisely from these areas, especially at the cardia when the endoscope is in the retroflexed position. In addition, when the tumors were of the limitis plastica type or were recurrent, they were more likely to yield non-diagnostic tissue. Recurrent tumors tend to be infiltrative in type.

Brush cytology alone provided a greater diagnostic yield in this study than did biopsy alone. This has been the general experience for a variety of gastric tumors. Endoscopic brush cytology has been shown to be more accurate than blind gastric tube cytological lavage. Brushing localizes the malignant cells thereby providing fewer extraneous cells such as respiratory and proximal gastrointestinal tract cells, and the cells are generally better preserved than those obtained by lavage. In addition, the preparation of brush cytology slides is easier than slides prepared from lavage, and requires less cytotechnician screening time. Furthermore, lavage specimens seem to be unsatisfactory more often. Endoscopic lavage is more accurate than is blind tube lavage, but both are less productive than direct brush cytology and have the above disadvantages of lavage specimens. This has been our experience as well as that of others. Tube or endoscopic lavage is useful in those patients in whom a definite lesion is not seen endoscopically, where multiple lesions are seen, such as in polyposis, or where a diagnosis could not be made by endoscopic brush and biopsy techniques. We have obtained diagnosis by tube lavage in infiltrative lesions that have been non-diagnostic by endoscopic techniques. Bedine and Cocco have successfully employed vigorous pre- or postendoscopic lavage in the diagnosis of gastric cancer.

Cytological technique may fail to provide a diagnosis in some patients. This is usually a result of clinical failure rather than microscopical failure. The lesion may be primarily or entirely submucosal, in anatomical areas difficult to sample, covered by fibrinous exudate, or processed in a manner that does not preserve the cells well. When adequate numbers of malignant cells are obtained and fixed promptly in proper concentrations of alcohol, the experienced cytologist rarely has difficulty in making a proper diagnosis. False-positive diagnoses are also rarely made by the experienced cytologist and, when made, are often in patients with premalignant disease such as pernicious anemia, polyposis, or ulcerative colitis. It is likely that some of these patients have occult cancer not detectable by clinical methods. It is well established that some patients can have positive cytology from preinvasive carcinoma that is clinically undetectable for many years.

Biopsy accuracy has generally been correlated with the number of biopsies obtained in each patient. Kasugai and Kobayashi recommend that three to five specimens be obtained from each lesion. Others have suggested that five or possibly six biopsies may be essential to provide the maximum diagnostic yield. For gastric ulcers, a minimum of six biopsies around the rim is critical. The average biopsy yield of experienced endoscopists is approximately 85% when four to six biopsies are obtained in each patient. The yield usually increases with experience. In one series, the yield increased from 45 to 88% over a number of years. The overall yield in our series probably reflected to some extent the endoscopic approach based on
an endoscopy team consisting of a trainee and an experienced attending gastroenterologist. The overall yield probably reflected to a greater extent the large number of cancers in difficult anatomical locations, the large number of infiltrative types, especially limitis plastica, and the large number of recurrent infiltrative cancers. The particular spectrum of advanced cancers included in this study undoubtedly is a result of the referral nature of the institution.

It would appear, therefore, that currently available fiberoptic endoscopes in general provide a fairly high degree of diagnostic accuracy for certain types of gastric cancers. Addition of cytological techniques has also increased the diagnostic yield. However, there are difficulties in diagnosis with certain types of advanced cancers and in certain anatomical locations. Japanese investigators have long recognized this and have developed a working classification to provide a basis for meaningful reporting. No such classification exists in this country. The gross morphological typing of gastric cancer has long been recognized as difficult and often unsatisfactory.

We simply divided tumors seen endoscopically into two major groups: exophytic mass lesions; and infiltrative lesions. A third obvious category, not included in this report because of low numbers, is the malignant ulcer. The Borrmann classification has been occasionally used in this country in describing endoscopic appearances of tumor. In 1926, Borrmann introduced a morphological classification of four main tumor types designed to help assign clinical behavior patterns to the types described. Type I is the polypoid or fungating variety; type II is a tumor mass which is ulcerated; type III is an infiltrating lesion which is ulcerated; and type IV is a diffuse infiltrating lesion.

A uniform endoscopic classification appropriate for the type of advanced gastric cancer seen in this country would be helpful in the interpretation of presented observations and data.

REFERENCES


16. Classen M, Rösch W: Gastroscopy, biopsy and